A non-unitary view of aging

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Chapter 2

TYPOLOGY OF COGNITIVE AGING
in a mixed group of younger and older adults

Experimental Study

Submitted

Typology of cognitive aging in a mixed group of younger and older adults

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Effects of aging on cognition are highly variable between individuals: some elderly even perform cognitively at the level of young adults. Identifying the variation in cognitive profiles associated with healthy aging is important for clinical decision making, particularly in dissociating "normal" age-related cognitive decline from decline predictive of or related to disease. In this study, graph-based community structure detection analysis was used to derive cognitive profiles from neuropsychological test scores in a mixed population of 79 young and 77 older adults. This approach, not assuming a-priori that younger and older adults have different cognitive profiles, resulted in six subgroups, each with a distinct pattern of neuropsychological performance. The stability of the identified subgroups was confirmed employing a support vector machine based analysis. We generally found age dependent cognitive profiles. However, 16 younger and 15 older adults shared a cognitive profile (the 'mixed' profile) of overall good cognitive performance with slightly decreased processing speed. Between the profiles that mainly belonged to either younger or older adults, we also found variability. The two 'younger' profiles both showed overall good cognitive performance while one profile was characterized by underperformance in phonemic and semantic fluency and the other by decreased phonemic fluency and working memory span. Only one 'older' profile was characterized by overall cognitive decline; the other two 'older' profiles showed cognitive domain-specific decline or cognitive performance in the range of younger adults, with the exception of immediate and delayed recall. Our approach of clustering in a mixed group of young and older adults shows that aging is not necessarily associated with cognitive decline and that being young is not necessarily associated with superior cognitive performance. The cognitively better performing elderly had a significantly higher level of education attainment and higher crystallized intelligence than the other elderly, which suggests that older adults with a higher cognitive reserve may be able to cope better with age-related neurobiological decline.

2.1 Introduction

Healthy aging has generally been associated with a decline in cognitive task performance[1-3]. However, the trajectory and degree of age-related cognitive change varies considerably across individuals. Both interindividual variability in cognitive performance (on a single task and occasion, referred to as 'diversity'[4]) and intraindividual variability in cognitive performance (on multiple tasks, referred to as 'dispersion' or on a single task on multiple occasions, referred to as 'inconsistency') increase with age[5,6]. Only few studies have investigated variability of elderly, combining diversity and dispersion. Such studies are necessary to more precisely characterize cognitive performance variability in the elderly and to better understand which patterns of cognitive decline are part of healthy aging and which are part of preclinical disease, which is especially useful in clinical decision-making[7]. In a recent study, Costa et al. (2013) divided older adults (50-89 years) into three groups of generally stronger, average and weaker cognitive performers[8]. In contrast, Gunstad et al. (2006), found distinct performance profiles across cognitive performance across tasks and across cognitive domains in the groups they distinguished[9]. In their subsample of 84 older adults (50-82 years), one group showed impaired executive functioning, a second group performed poorly in tasks measuring processing speed while a third group showed a more general decrease in overall cognitive performance. Similar results were found by Ylikoski et al (1999) who identified subgroups with homogeneous cognitive test performance in a group of 120 neurologically healthy older (55-85 years) adults[10], by Maxson, Berg and McClearn (1997) who assessed the diversity of aging across cognitive, as well as physical, functional and social domains in 335 70-year olds[11], by Ritchie et al. (1996) who differentiated subtypes of cognitive impairment in 397 elderly with recent cognitive deterioration[12], and by Foss et al (2009) who specifically assessed cognitive typology in a group of 60 elderly with different socioeconomic backgrounds[13]. As may be concluded from the preceding discussion, most previous studies examining variability in cognitive aging across tasks have focused on the old[8,10-13] or have used an a-priori division of their research population in different age categories[9]. It is important to note that variability in cognitive performance among the elderly might be explained by factors that are already present at younger ages. For example, genetic modulation of cognition[14,15] or of dopamine receptors[16,17] may influence cognitive performance variability, also in younger adults. The influence of these factors might, however, change with age. Neurobiological differences[18] and decline in the efficiency of executive control[19], for example, are thought to increase cognitive performance variability with advancing age. In addition to these internal factors that may underlie variability in cognitive performance, environmental factors such as socioeconomic status, education level and intelligence quotient (IQ) might influence cognitive performance, as well[20], and especially these factors are thought to allow some to cope better with the neural and cognitive decline in the aging brain, than others (cognitive reserve theory[20-22]). Indeed, high levels of cognitive performance in older adults have been associated with higher levels of education attainment and higher levels of vocabulary knowledge[13,23]. To obtain a complete typology of cognitive aging that takes into account that individual trajectories of cognitive aging may not be just related to age, we here derive such a typology in a mixed group of young and older adults. Variability in cognitive performance is generally derived from compound neuropsychological test results. Such tests are frequently used in scientific and clinical settings to evaluate functioning across a variety of cognitive domains. The current study aimed at extending previous knowledge on the diversity and dispersion in cognitive performance, employing results obtained on a clinically employed, neuropsychological test battery. In addition to the advantage of our approach not assuming a-priori that younger and older adults have different cognitive profiles, its results also have direct clinical impact by focusing on tests particularly used in clinical settings.

To identify cognitive typologies based on neuropsychological test results various clustering techniques have been applied. In general, the methods that have been applied can be divided in three well-known classes of clustering methods: 1) the hierarchical methods, that cluster data points on the basis of distance connectivity (e.g., Ward's method[11,24] or linkage hierarchical methods[11,24]), 2) the centroid methods that represent clusters by a central data point, that may not be part of the dataset (e.g., K-means clustering[9,10,25]), and 3) the distribution-based methods that define clusters as data points most likely belonging to the same distribution (e.g., Bayesian latent class analysis[8]). Although all clustering methods have their advantages and disadvantages, with the more recent advances in graph theory, the first mentioned hierarchical methods have benefited since distance connectivity has a natural counterpart in graphs.

Graphs are sets of nodes or vertices connected by lines or edges. By applying a cut-off to a measure of similarity between data points (that will function as nodes in a graph), data points can be said to be connected (high similarity) or disconnected (low similarity). Based on such a connectivity pattern, a graph can be constructed for any data set. Then, as a means of clustering the original data points, community detection can be applied to the graph. Community detection identifies groups of nodes in a graph that are more densely connected internally than with the rest of the graph. When a dataset is converted to a graph by defining connectivity between data points on the basis of a distance (or ssimilarity) measure, different community detection methods can be applied to cluster the original dataset. One of the most widely used methods for community detection is modularity maximization[25]. Modularity is a graph-theoretic measure that quantifies the quality of a particular division of a network into communities (i.e. clusters). However, modularity maximization is a very computationally intensive process when an exhaustive search is used. One of the most efficient alternative methods today is the method proposed by Newman (2006)[26] which reformulates modularity in terms of the spectral properties of a network. Since its inception this method has been amply used, but its application in identifying cognitive typologies has been limited to a study in typically developing youth and children with ADHD[27], as far as we know. Because of its advantages (the network and not the experimenter defines the clusters and the method is fast[26]), we applied this method to identify cognitive typologies in a mixed group of young and older adults.

In our application, the graph consists of nodes reflecting participants and connections between them, indexing the similarity of cognitive test performance. Because we know that cognitive aging is a highly variable process and that some elderly perform cognitively on the same level as their younger counterparts, we hypothesize that the chosen method applied to a group consisting of both young and older adults will identify at least one mixed subgroup of cognitively similarly performing younger and older participants. In addition, we also expect that several older adults will be separated from the young adults, in line with theories of general cognitive decline with age. Furthermore, the stability of the subgroups identified by community detection is validated by a support vector machine based analysis. This approach allowed investigating how well individual participants were assigned to the subgroups defined by the community detection analysis. We also investigated whether broad measures of functioning (education attainment and estimates of intelligence) that were not included in the determination of cognitive typologies, were related to group membership of individual participants.

2.2 Materials and Methods

2.2.1 Participants

Neuropsychological data from 158 healthy adults (mean age 42.5 years; range 18 - 74 years; 79 males) was evaluated for this study. Eighty participants were younger adults (mean age 20.2 years; range 18 - 26 years; 41 males) and 78 participants were older adults (mean age 65.3 years; range 59 - 74 years; 38 males). Participants were recruited through advertisements in local newspapers. All participants were right handed and had normal or corrected to normal visual acuity. Exclusion criteria were a history of neurological, psychiatric or vascular disease and use of any psychotropic medication. To verify normal cognitive functioning, the MMSE[28] and the HADS[29] were used. Only participants who scored above 26 on the MMSE and below 16 on each of the subscales of the HADS were included. One younger and one older participant did not complete all neuropsychological tests and were excluded from further analysis. In addition, one older participant was excluded due to brain abnormalities discovered in the anatomical scan collected for other purposes. The local ethics committee approved the current study. All participants gave written informed consent.

2.2.2 Neuropsychological testing

Participants were tested on a clinical neuropsychological test battery that encompassed tests for different aspects of cognitive functioning, such as processing speed, executive functioning, verbal fluency, working memory span, recall and recognition, and response speed. To assess cognitive processing speed, the trail making tests A and B were used. The trail making B test has also been associated with executive functioning[30]. Participants were instructed to execute the tasks as quickly as possible. Each test was practiced prior to the assessment. These tests were scored by the time taken to complete the test, including the time it took to correct the (possible) errors made. Verbal fluency was assessed by four subtests. For two of these subtests (phonemic fluency), participants had to generate as many meaningful words as possible beginning with 1) the letter "S" and 2) the letter "F" in 60 seconds. For the remaining subtests (semantic fluency), they were instructed to generate as many 1) professions and 2) animals as possible within 60 seconds. The order of the phonemic and semantic subtests was semi-randomized between participants. The score on each of the fluency tests was the number of correct words. The digit-span tests forward and backward were used to assess working memory span. The score on each of the tests was the maximum number of correctly recited digits. The 15 words test was used to assess immediate and delayed recall as well as recognition. The immediate recall consistent of five blocks of trials: in each block the participants were required to recall as many words as possible, immediately after they were presented to them. The delayed recall and the recognition subtests consisted of one block each. For each of the three subtests, the score was the number of correctly remembered words. Finally, response speed was assessed by means of a simple reaction time test, in which participants were required to press a response button as quickly as possible whenever a red dot appeared on the screen. The red dot remained on screen for 300 ms and intertrial intervals (ITI) varied randomly between 2000 and 6000 ms. Response speed was scored as the median response time (RT) for correct button presses.

2.2.3 Variable selection

To identify variability in performance on the neuropsychological tests the following 8 compound scores were taken into account for further analysis: 1) phonemic fluency (mean score on the subtests "S" and "F"), 2) semantic fluency (mean score on the subtests "professions" and "animals"), 3) working memory span (mean score of the digit-span forward and backward tests), 4) trail making A score (time to complete the trail making A test), 5) trail making B/A score (time to complete the trail making B divided by the time to complete trail making A test), 6) immediate recall (sum of recalled items in the 5 sessions of the immediate recall subtest), 7) delayed recall score and 8) response speed score. The recognition score for the 15 words test was excluded for further analysis; due to the lack of variability among participants inclusion of this test would not add relevant information to the identification of cognitive profiles.

2.2.4 Subgroup identification: community structure detection

All compound scores were transformed to z-scores. Subsequently, to ensure that a higher score was equivalent to better performance scores were multiplied by -1 if necessary. To be able to apply community detection as a form of hierarchical clustering, we first determined the graph describing the relation between participants based on their cognitive test performance. Each of the participants forms a node in the graph. To determine whether there was a connection between nodes (i.e. similarity in cognitive test performance between participants/nodes), we determined similarity of the selected cognitive test scores between each pair of participants by calculating the intraclass correlation coefficient ICC (A,1)[31], for each pair of participants across test scores. Subsequently, a square symmetric ICC matrix (155 x 155) was constructed, containing the ICC values for each pair of participants in the population. To determine whether a pair of participants was connected – that is whether similarity was high enough - the ICC matrix was thresholded such that a participant was connected via at least one path to every other participant in the population (the graph was "strongly connected" or "reachability" was 1; see Fair et al. (2012)), resulting in a threshold of 0.3870. Because the chosen threshold potentially has a large impact on the detected communities[32], the robustness of the detected communities was further investigated for different (lower) thresholds (ICC=.3, ICC=.2, ICC=.1). For higher thresholds, the reachability of the resulting graph would be lower. We found that the number and size of identified communities was independent of the chosen threshold. To identify the communities (i.e. clusters) in our graph, the modularity (Q) maximization approach of Newman (2006)[2] was used. Newman's algorithm aims at identifying communities in a network, which share fewer edges between each other than would be expected in a network with an equivalent degree of distribution, in which edges are placed at random. Q quantifies the difference between the actual connections in the network and the expected connections in the equivalent random network; a positive Q thus indicates that the number of edges within communities is higher than expected in the equivalent random graph.

2.2.5 Cluster stability and validation

Participants were assigned to separate clusters using community detection analysis. Because the cluster assignment within this method is deterministic, there is no information on how stable the clusters are and how well a new individual can be captured within the existing clusters or classified as member of the existing clusters. To determine cluster stability, and indicate how well new individuals can be classified as member of the existing clusters, we used a support vector machine (SVM) with a radial basis function (RBF) kernel, provided in the package LIBSVM[33] *(http://www.csie.ntu.edu.tw/~cjlin/libsvm/)*. An SVM is an algorithm that can find patterns within measured variables in order to categorize data. Typically, an SVM is trained on a number of entities (in this case participants) described by a set of defining variables (in this case compound neuropsychological test scores) and their associated class label of each entity (in this case label of the cluster identified by community detection analysis the participant was assigned to). Within the training part, the SVM associates patterns among the variables with the class labels. The result is captured in a model, which is able to classify new entities to the existing class labels (see Burges (1998)[34] for an extensive overview of SVM). The performance of an SVM prediction is often expressed in terms of sensitivity and specificity. Sensitivity refers to how well a class can be predicted and is calculated by the number of true positives in the prediction divided by the total number of true class members. The specificity refers to how specific a group was in the prediction results and is calculated by the number of true negatives in the prediction divided by the total number of other class members.

To assess the SVM prediction performance on the clusters that were produced using community detection analysis, we performed two cross-validation procedures; leave one out cross validation (LOOCV) and dataset partitioning[35]. In LOOCV, data from one participant is used as testing dataset, while data from the remaining participants forms the training data. This procedure is repeated until data from each participant has been used once for testing purposes. Because LOOCV can give an optimistic result, we also determined the cross-validation results of dataset partitioning. In this procedure, every subgroup identified through community detection analysis was divided in two parts of (almost) equal size. One of these parts was used for training while the other part was used for testing purposes.

We also investigated whether broad measures of cognitive functioning that were not included in the determination of cognitive typologies (i.e. measures not included in the clinical test battery that was used), were related to group membership of individual participants. For this purpose we employed the level of education attainment, estimates of fluid and crystallized intelligence, as well as scores on the digit symbol coding test. The latter test employs 9 pairs of numbers and abstract symbols. First, participants memorized the number-symbol pairing and practiced briefly. Subsequently, participants were asked to write down the corresponding symbols under a sequence of numbers, as quickly as possible within 120 seconds. An estimation of crystallized intelligence was obtained through the Dutch Adult Reading test[36], which is the Dutch version of the National Adult Reading Test (NART) and requires participants to read aloud a list of words, with irregular pronunciation. An estimate of fluid intelligence was obtained from the WAIS-matrix reasoning test in which participants are presented with 26 incomplete patterns (or matrixes) and are required to select the response that completes each pattern[37]. Subgroup differences on these variables were tested by univariate ANOVA (significance level α=.05). To estimate education attainment four levels were distinguished: 1) lower education, 2) lower-technical and vocational training and lower general secondary education or preparatory middle-level applied education, 3) vocational training and higher general continued education or preparatory scholarly education and 4) higher professional education or university level. To investigate subgroup differences in education level, chi square (X2) testing was performed.

2.3.1 Community detection

Community detection analysis resulted in 6 separate communities/clusters or subgroups (Figure 2.1A and B), at a modularity maximization index (Q) of 0.49. Two of these subgroups consisted mainly of younger adults (young/old; Subgroup (S) 1: 23/0 and S2: 35/4). One 'mixed' subgroup contained comparable numbers of younger and older adults (S3: 16/15). The remaining three subgroups were dominated by older adults (S4: 2/24, S5: 1/10 and S6: 2/26) The SVM classifier, used to determine how well participants were assigned to the subgroups identified by community detection analysis, showed that there was a strong distinction between these groups (overall classifier accuracy: LOOCV: 83.9% and data partitioning: 74.7%). The sensitivity and specificity of both analyses for each of the subgroups are presented in Table 2.1.

Table 2.1 Sensitivity and specificity of the SVM algorithm for each subgroup, for the LOOCV method and the data partitioning method, separately.

Subgroup		LOOCV		Data partitioning[1]	
	Size	*Sensitivity*	*Specificity*	*Sensitivity*	*Specificity*
S1	23	82.6	99.2	83.3	100
S2	39	89.7	94.1	65	98.1
S3	31	87.1	92.3	93.3	84
S4	26	85.6	96.9	84.6	92.8
S5	11	81.8	99.3	83.3	100
S6	25	72	98.4	46.2	96.7

[1]For the data partitioning procedure, the training dataset consisted of 76 participants: S1(11), S2(19), S3(16), S4(13), S5(5) and S6(12). The testing dataset consisted of 79 participants: S1(12), S2(20), S3(15), S4(13), S5(6) and S6(13).

Figure 2.1 A. Graph representation of the subgroups resulting from community structure identification, using the build-in layout Force-Atlas method in Gephi, version 17[38]. This method employs a spring-directed algorithm that assumes two competing forces, a repulsive force driving all nodes apart and an attractive force ('spring force') keeping the nodes linked by edges together. The stronger the connection (similarity), the stronger the attractive force and the closer the edges will be in the visualization. ***B.*** Table representing the number of younger and older adults in each subgroup. ***C.*** Boxplots representing scores for each subgroup for each of the neuropsychological tests.

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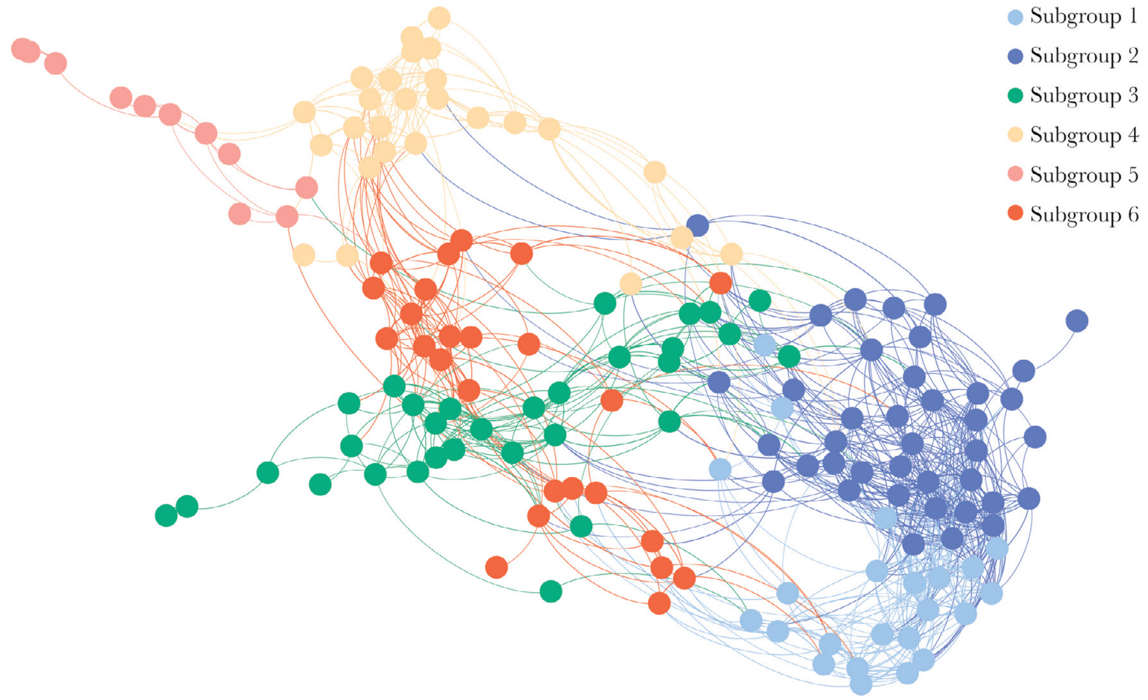
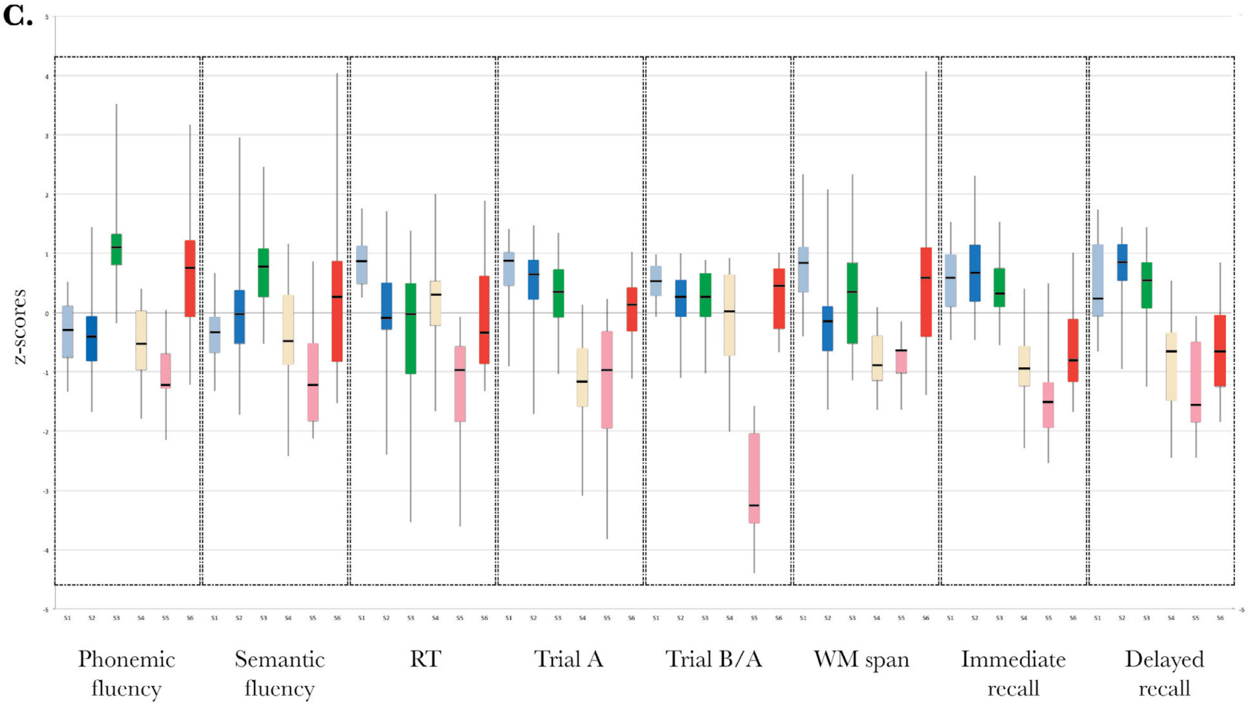
A.

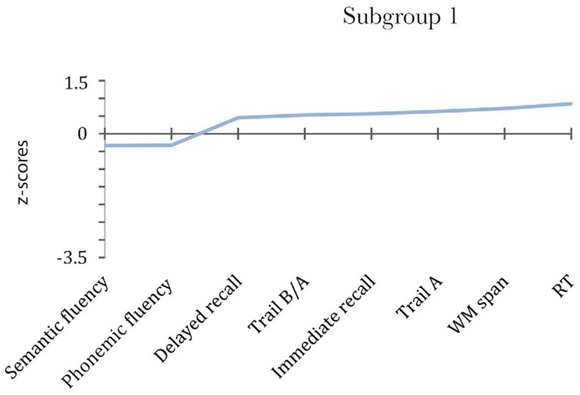


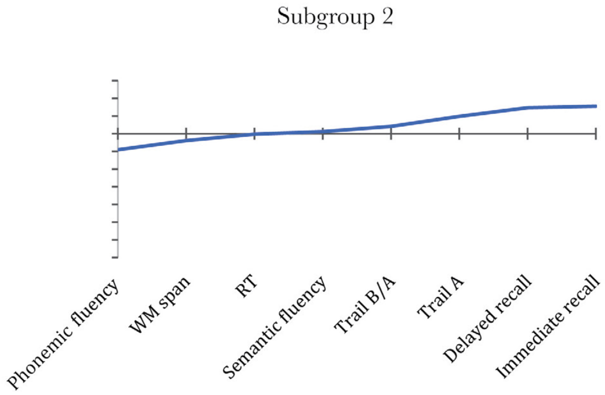
B.

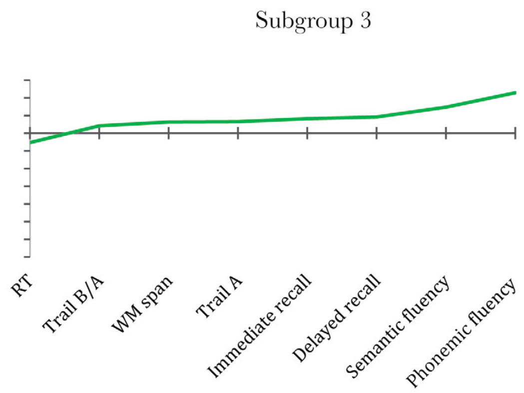
	Subgroup 1	Subgroup 2	Subgroup 3	Subgroup 4	Subgroup 5	Subgroup 6
Young	23	35	16	2	1	2
Old	-	4	15	24	10	23

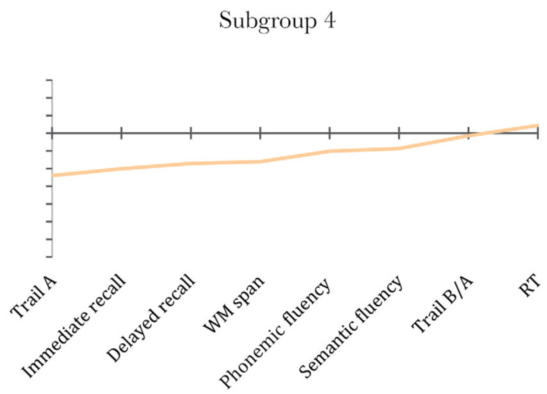
C.

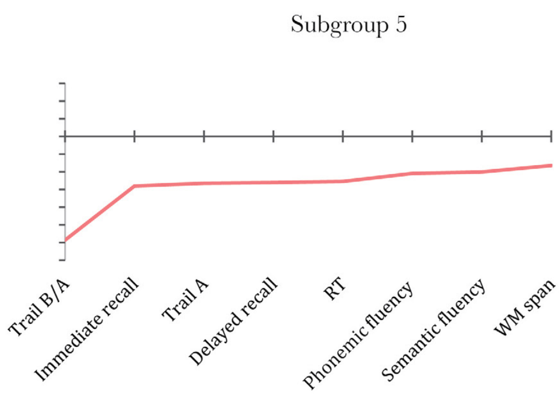


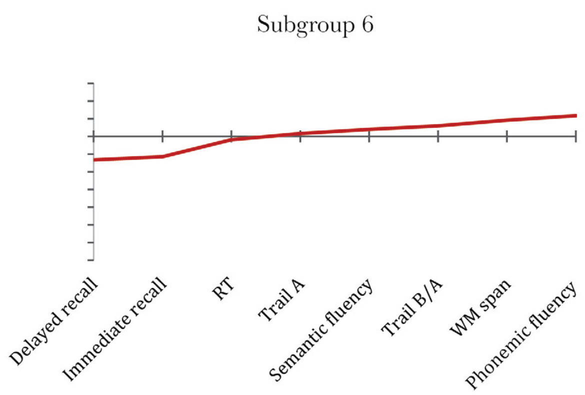

Subgroup 1
1.5
0
-3.5
z-scores
Semantic fluency
Phonemic fluency
Delayed recall
Trail B/A
Immediate recall
Trail A
WM span
RT


Subgroup 2
Phonemic fluency
WM span
RT
Semantic fluency
Trail B/A
Trail A
Delayed recall
Immediate recall


Subgroup 3
RT
Trail B/A
WM span
Trail A
Immediate recall
Delayed recall
Semantic fluency
Phonemic fluency


Subgroup 4
Trail A
Immediate recall
Delayed recall
WM span
Phonemic fluency
Semantic fluency
Trail B/A
RT


Subgroup 5
Trail B/A
Immediate recall
Trail A
Delayed recall
RT
Phonemic fluency
Semantic fluency
WM span


Subgroup 6
Delayed recall
Immediate recall
RT
Trail A
Semantic fluency
Trail B/A
WM span
Phonemic fluency

The cognitive profile of subgroup 1 (young, 14.8% of the total population) was characterized by a below average performance on verbal fluency tests and above average compound scores on the remaining neuropsychological tests. Participants in subgroup 2 (mostly young, 25.2% of the population) performed above average on tests related to executive functioning (trail making A and B/A) and memory (immediate and delayed recall), but average or below average on tests related to verbal fluency, working memory span and RT. Participants in subgroup 3 (mixed age, 20 % of the population) were slower than average (RT), but had above average compound scores on the remaining neuropsychological tests. In contrast, participants in subgroup 4 (mostly old, 16.8% of the population) were faster than average (RT), but had below average compound scores on all remaining tests. The cognitive profile of participants in subgroup 5 (mostly old, 7.1% of the population) was characterized by overall decreased compound scores, particularly on the trail making B/A test that is thought to provide a measure of executive functioning. Participants in subgroup 6 (mostly old, 16.1% of the population) had lower compound scores on tests measuring aspects of memory (delayed and immediate recall), but average or above average compound scores on the remaining tests.

<< ***Figure 2.1 D.*** Compound neuropsychological test scores (mean), separately, for each of the six subgroups. Note that the order of the tests on the x-axis differs between subgroups, because they are ordered by increasing z-score.

2.3.2 Differences in demographics and broad measures of cognitive functioning between subgroups

Demographics and broad measures of cognitive functioning (level of education attainment, estimates of fluid and crystallized intelligence, scores on the digit symbol coding test) are presented in Table 2.2, separately for each subgroup. There were no differences in mean age between the younger subgroups (S1 and S2) or between the older subgroups (S4, S5 and S6). We also analysed differences in age distribution between subgroups, separately for younger and older adults within the groups. Only two subgroups differed with respect to the age of the older participants within the subgroup; older participants in S5 were on average older than older participants in S3 ($F(4,71)=3.2$; $p=.019$). The young adults in each subgroup had comparable age. There were no differences in MMSE scores between the subgroups dominated by younger adults or between those dominated by older adults. However, participants in the younger (S1 and S2) and mixed subgroup (S3) had higher MMSE scores than participants in the older subgroups (S4-S6, $F(5,149)=13.8$; $p<.005$; illustrated in Figure 2.2A). The six subgroups had similar scores on both the anxiety ($F(5,149)=.84$; n.s.) and the depression ($F(5,149)=1.7$; n.s.) subscales of the HADS test. Participants in mixed subgroup S3, had higher crystallized IQ scores than participants in the two younger subgroups (S1 and S2) and in one older subgroup (S5). Among the three 'predominantly' older subgroups, participants in S5 had the lowest and participants in S6 had the highest crystallized IQ scores ($F(5,149)=12.6$; $p<.0005$; Figure 2.2B). In general, participants in S5 had lower fluid IQ scores than participants in S1, S2, S3 and S6 ($F(5,149)=5.1$; $p<.0005$). Participants differed in their performance on the digit symbol coding test between subgroups ($F(5,149)=17.7$, $p<.0005$; Figure 2.2C). Participants in S1 and S2 had higher scores than all three older groups (S4, S5 and S6). Among these older groups, participants in S6 performed best at the digit symbol coding test. Finally, participants in S6 also attained a higher education level than participants in the other older subgroups S4 ($X2\ (51)=8.1$, $p=.017$) and S5 ($X2\ (36)=11.7$, $p=.007$; see Figure 2.2D).

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Table 2.2 Demographics and broad measures of functioning for each subgroup.

	S1	S2	S3	S4	S5	S6
N	23	39	31	26	11	25
Young/Old	23/-	35/4	16/15	2/4	1/10	2/23
Male/Female	13/10	17/22	12/19	15/11	5/6	16/9
Age (years): young (median(range))	19(18-23)	20(16-24)	20.5(18-26)	19.5(18-21)	19(19)	21(20-22)
Age (years): old (median(range))	-	62.5(59-69)	63(60-70)	65.5(60-74)	68(62-74)	64(60-72)
MMSE (mean(SD))	29.4(0.7)	29.5(0.6)	29.6(0.6)	28.4(1.1)	28.1(1.2)	28.5(1.1)
HADS anxiety (mean(SD))	3.8(1.7)	3.2(2.2)	3.9(2.8)	3.7(2.2)	4.6(2.7)	3.2(2.9)
HADS depression (mean(SD))	1.4(1.6)	1.8(1.9)	1.5(1.6)	2.3(2.6)	3(2.9)	1.6(1.2)
Crystallized IQ (mean(SD))	103.7(5.6)	102.3(4.9)	111(8.7)	105.2(10.4)	96.5(7.8)	114(9.3)
Fluid IQ (mean(SD))	113(12.6)	111.2(10)	111.6(9.1)	106.5(8.6)	97.3(9.3)	111(9.2)
Digit symbol coding (mean(SD))	86(12.7)	83(15.1)	79.5(14)	60.5(8.3)	56.2(13.5)	72.6(13.3)
Education attainment level (1/2/3/4)	-/-/18/5	-/-/24/15	-/-/11/20	-/7/6/13	1/3/5/2	-/-/10/15

S=Subgroup; Education level: 1=lower education; 2= lower-technical and vocational training, lower general secondary education or preparatory middle-level applied education; 3= vocational training, higher general continued education or preparatory scholarly education, 4= higher professional education or university level.

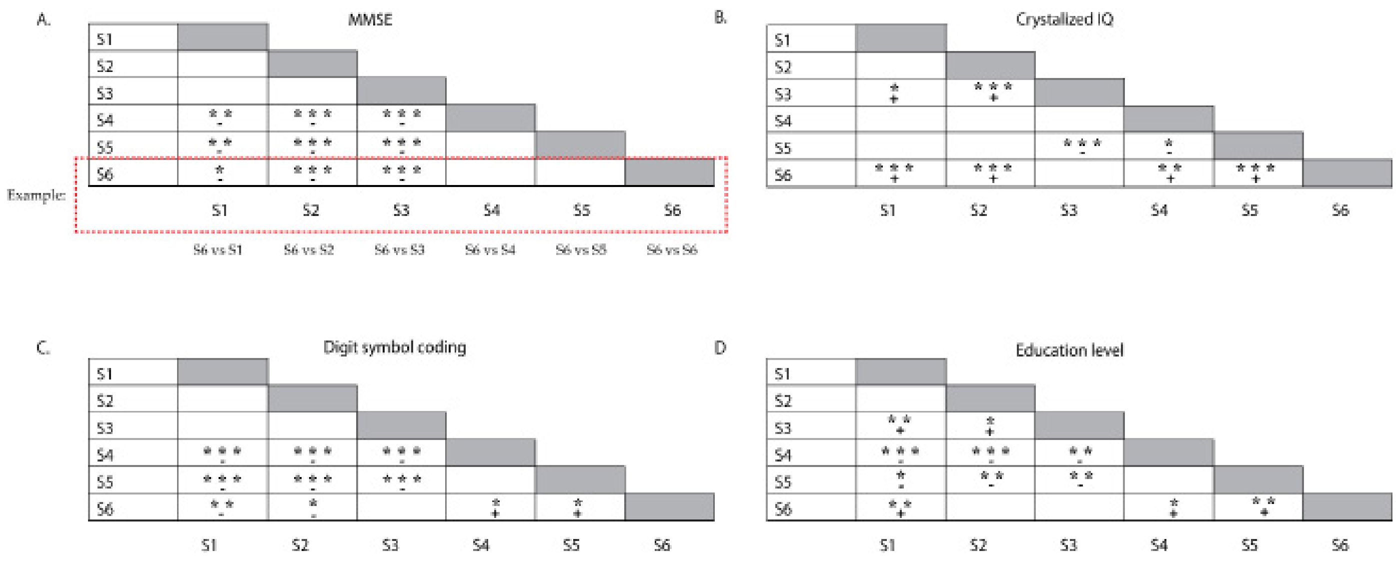

Figure 2.2 Illustration of the differences between subgroups, for ***A.*** the MMSE test results, ***B.*** crystallized IQ scores, ***C.*** Symbol coding test scores and ***D.*** education level. Groups represented in each row were compared with the subgroups represented in each column (e.g. S6 (row) vs. S1 (column), S6 vs. S2 (column); see example given); +: reflects a positive mean difference ('row' group larger than 'column' group) between the subgroups, −: reflects a negative mean difference ('row' group smaller than 'column' group) between the subgroups; *:p<.05; **:p<.01; ***:p<.001.

2.4 Discussion

In the current study, we investigated variability (diversity and dispersion) in cognitive performance with the aim to derive cognitive profiles in a mixed population of young and older adults. Cognitive profiles were identified by community detection analysis[26] on compound scores obtained from a clinically employed neuropsychological test battery. The robustness of the resulting subgroup partition was confirmed by two SVM-based approaches. We hypothesized that our approach would identify at least one age-mixed subgroup of cognitively similarly performing participants and additional subgroups in which older adults would be separated from the young adults, in line with theories of general cognitive decline with age.

Indeed, we identified a mixed subgroup of older and young participants who performed at a similar cognitive level, showing overall good cognitive performance with slightly decreased processing speed. We also found subgroups which mainly consisted of either younger or older adults. These age-characterized subgroups varied with respect to their cognitive profiles. The two 'younger' profiles showed overall good cognitive performance while one profile was characterized by underperformance in phonemic and semantic fluency and the other by decreased phonemic fluency and working memory span. Only one 'older' profile was characterized by overall cognitive decline; the other two 'older' profiles showed cognitive domain-specific decline or cognitive performance in the range of younger adults, with the exception of immediate and delayed recall. The presence of three older profiles and only two younger profiles may reflect increased performance variability in the elderly[5,19]. Our approach of clustering in a mixed group containing both young and older adults shows that aging is not necessarily associated with cognitive decline and simultaneously, that being young is not necessarily associated with superior cognitive performance. We also found that the cognitively better performing participants in older subgroup 6 had a significantly higher level of education attainment and higher crystallized intelligence than the participants in the other older subgroups 4 and 5[10,13]. Participants in this subgroup also had higher scores on the digit symbol coding test than participants in the other older subgroups. The digit symbol coding test draws on several cognitive functions, such as visuomotor coordination, sustained and selective attention and associative learning[30]. Age by itself can not explain the differences between the older subgroups on these broad measures of cognitive functioning as the age distribution of the elderly in subgroups 4, 5 and 6 was comparable. Therefore these results seem to suggest that older adults with a higher so-called 'cognitive reserve', as reflected in higher educational attainment and crystallized intelligence level, may be able to cope better with age-related neurobiological decline.

The cognitive reserve theory[20,21] proposes that higher education level and IQ scores are protective factors that allow certain individuals to compensate for neural decline in the aging brain. More specific, the cognitive reserve theory postulates that the differential recruitment of typical brain networks or the additional recruitment of other, compensatory, networks gives rise to the variability in task performance in the elderly[21,22]. Park and Reuter-Lorenz (2009) also elaborate on the efficient recruitment of additional neural networks, which they call scaffolding networks or scaffolds[2]. In their scaffolding theory of aging and cognition (STAC), they argue that older adults showing high levels of cognitive functioning make effective use of scaffolding networks to maintain task performance. However, the link between life factors such as education and IQ on one hand and cognitive performance on the other should be interpreted with caution. Until now, longitudinal studies have failed to find a reliable association between higher education and stability of cognitive performance with increasing age[39,40]. Nevertheless, an intriguing question is whether the cognitive profile observed in the poorest performing older subgroup (S5) is just a facet of healthy aging, or whether decline in function exceeds the respite offered by compensatory strategies in participants in this group and that participants in this group are at a higher risk for developing mild cognitive impairment (MCI) or dementia. One of the criteria for an MCI diagnosis is objective memory impairment for age, which is often conceptualized as performing 1.5 SD below the performance of age-mates[41]. Although participants in our subgroup 5 performed well below average on the neuropsychological tests included in the community detection analysis they did not perform particularly worse at the included measures of memory for which their z-scores were above -1.5. Their MMSE scores did not differ from those of the other older subgroups either. Therefore, additional (longitudinal) information is needed to examine transition stages from healthy aging to aging-related neurodegenerative disorders. To this end, measures of differences in underlying neural activity may help to better understand performance variability among these 'older' subgroups[2,42,43]. Variability in cognitive performance was also observed in the young population. In particular, the younger subgroups showed consistently high performance on all but the verbal fluency tasks. It is known that younger adults generally have lower vocabulary knowledge than older adults[44], which probably explains their reduced capacity to generate words based on their semantic or phonetic properties. As an interesting consequence of our approach to determine cognitive profiles in a mixed population of young and older adults, some younger participants were classified in 'older' subgroups with poor cognitive performance (S4 and S5), indicating that efficient cognitive performance does not characterize all younger adults. Our results confirm the presence of cognitive performance variability not only among older, but also among younger adults. As such, conclusions based on averaged performance levels in both young and old groups may obscure existing variability in cognitive functioning in either age group.

In summary, employing graph-based clustering applied to compound neuropsychological test scores obtained in a large mixed group of both young and older adults, six subgroups were identified characterized by distinct cognitive profiles. By taking this approach, we identified one subgroup with comparable numbers of younger and older adults, confirming that some elderly perform cognitively at the level of young adults. Two of the subgroups were dominated by younger adults and three subgroups were comprised mainly of older adults, in line with expectations that cognitive profiles generally differ as a function of age. However, only a small proportion of older participants showed impaired cognitive performance across all tested cognitive domains. Most older participants showed either a moderate decline in performance or successful performance depending on the test at hand. These findings provide more evidence that the notion of inevitable cognitive decline with age is too simple.

Aging is not a unitary process and cognitive decline - as our study illustrates - can become apparent in variable patterns across cognitive domains, possibly because neuronal decline varies across brain areas for individuals. The mapping and understanding of cognitive profiles associated with aging may be of importance to clinical decision-making, particularly when trying to understand differences in performance decline related to normal aging and those associated with, or predictive for, disease.

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